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EXAMINER

RAMIREZ, DELIA M

ART UNIT PAPER NUMBER

1652

DATE MAILED: 02/10/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

**Application No.**

09/577,005

**Applicant(s)**

ASAKURA ET AL.

**Examiner**

Delia M. Ramirez

**Art Unit**

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 21 November 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 20-37 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 20-37 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some \* c) ☐ None of:
- 1) ☒ Certified copies of the priority documents have been received.
  - 2) ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - 3) ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date <u>11/21/03-9/2/03</u> | 6) <input type="checkbox"/> Other: _____  |

## **DETAILED ACTION**

### ***Status of the Application***

Claims 20-37 are pending.

Applicant's cancellation of claims 1-19, addition of claims 20-37, amendments to the specification, and submission of a new abstract, in a communication filed on 8/12/2003 are acknowledged.

Applicant's submission of a new sequence listing in paper and electronic form, amendments to claims 20, 23, 33, amendments to the specification, and submission of references by Mansi et al. and Alvarez-Villafane et al., in a communication filed on 11/21/2003, are acknowledged.

Applicants submit that due to an obvious clerical error, the term "isocitrate synthase" is not the correct designation for the term "ICDH" but rather "isocitrate dehydrogenase". Applicants refer to the specification and the references by Mansi et al. and Alvarez-Villafene et al. in support of amendments to the specification and claims, which now recite "isocitrate dehydrogenase" instead of "isocitrate synthase". Applicant's arguments have been fully considered and are deemed persuasive in regard to amendments which replace the term "isocitrate synthase" with "isocitrate dehydrogenase" in the claims and the specification. Thus, the amendments submitted have been entered.

Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

### ***Information Disclosure Statement***

1. The information disclosure statements (IDS) submitted on 9/2/2003 and 11/21/2003 are acknowledged. Only the abstract of reference AP (IDS filed 9/2/2003) has been considered since the remainder of the document is not in English. While the Examiner acknowledges the submission of reference AO in an IDS filed on 9/2/2003, it is noted that only the title of the reference has been considered since the remainder of the document is not in English. The remaining references in the

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submissions are in compliance with the provisions of 37 CFR 1.97 and are being considered by the Examiner.

### *Specification*

2. The amendment filed on 11/21/2003 is objected to under 35 U.S.C. 132 because it introduces new matter into the disclosure. 35 U.S.C. 132 states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows: the sequence listing submitted contains 66 sequences. The sequence listing as originally filed contains 64 sequences. No explanation has been provided as to how the specification provides support for the additional sequences or what these sequences are. In addition, Applicants have not provided any information as to which is the numerical correspondence between the old sequence identifiers and the new ones. Applicant is required to cancel the new matter in the reply to this Office Action or provide clarification/support for the amendments.

3. The amendment filed on 11/21/2003 is objected to under 35 U.S.C. 132 because it introduces new matter into the disclosure. 35 U.S.C. 132 states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows: the new sequence listing indicates that SEQ ID NO: 64 contains a "g" instead of an "f" as originally filed (SEQ ID NO: 62) at position 29. While Applicants (Reply filed on 11/21/2003) submit that "f" is not a base and was introduced by a typographical error, no support has been presented for replacing "f" with a "g". The Examiner acknowledges that "f" is not an appropriate nucleic acid designator. However, in the absence of any supporting evidence, such as an alignment between SEQ ID NO: 64 and a previously disclosed *gdh* promoter region, teaching that a "g" is the correct base at position 29 of SEQ ID NO: 64, one cannot reasonably conclude that there is enough support for the amendment in

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said sequence. Applicant is required to cancel the new matter in the reply to this Office Action or provide clarification/support for the amendment.

***Claim Objections***

4. Claim 20 is objected to due to the recitation of “a promoter sequence of the glutamic acid...gene”. For clarity, it is suggested that the term be amended to recite “the promoter sequence of the glutamic acid....gene”. Appropriate correction is required.

5. Claims 26, 32, 34, and 36 are objected to due to the recitation of “gene of claim X further comprising TATAAT...”. For clarity, it is suggested that the term be amended to recite “gene of claim X further comprising a DNA sequence situated at....., wherein said DNA sequence is TATAAT ...” (claims 26, 32, 34) or “gene of claim X further comprising the DNA sequence TATAAT” (claim 36), to clearly indicate what TATAAT and CATAAT are. Appropriate correction is required.

***Claim Rejections - 35 USC § 101***

6. 35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

7. Claims 20-37 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

8. Claims 20-37, as written, do not sufficiently distinguish over nucleic acids and organisms as they exist naturally because the claims do not particularly point out any non-naturally occurring differences between the claimed products and the naturally occurring products. In the absence of the hand of man, the naturally occurring products are considered non-statutory subject matter. See *Diamond v.*

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*Chakrabarty*, 447 US 303, 206 USPQ 193 (1980). The claims should be amended to indicate the hand of the inventor, e.g., by insertion of “isolated” or “purified”. See MPEP 2105.

***Claim Rejections - 35 USC § 112, Second Paragraph***

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claims 20-37 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

11. Claims 20-25, 33, 35 (claims 26-32, 34, 36-37 dependent thereon) are indefinite in the recitation of “glutamic acid synthesizing gene selected from the group consisting of glutamate dehydrogenase, citrate synthase, isocitrate dehydrogenase, pyruvate dehydrogenase, and aconitase...” or “the glutamic acid synthesizing gene of claim 20, which is ...” for the following reasons. The items recited as part of the group (i.e. glutamate dehydrogenase, citrate synthase, isocitrate dehydrogenase, pyruvate dehydrogenase, and aconitase) are not genes but rather enzymes. For examination purposes, it will be assumed that the claims recite “a glutamic acid synthesizing gene encoding an enzyme selected from the group consisting of ...” or “the glutamic acid synthesizing gene of claim 20 wherein the enzyme is...”. Correction is required.

12. Claim 20 (claims 21-37 dependent thereon) is indefinite in the recitation of “DNA sequence situated at position –35 in a promoter sequence of the glutamic acid....gene” for the following reasons. As written, it is unclear which is the correlation between position –35 and the hexamers recited. One cannot determine if, for example, the hexamer CGGTCA is located in the promoter region such that (1) position –35 corresponds to the first base C, (2) position –35 corresponds to the last base A, or (3) position –35 corresponds to any of the bases in the hexamer. For examination purposes, it will be

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assumed that the term recites "DNA sequence selected from the group consisting of . . . , wherein said DNA sequence is centered at about position -35 in the promoter sequence. Correction is required.

13. Claims 26, 32, and 34 are indefinite in the recitation of "gene of claim X further comprising TATAAT . . . situated at position -10 in the promoter sequence" for the following reasons. As written, it is unclear which is the correlation between position -10 and the hexamer(s) recited. See discussion above regarding claim 20. For examination purposes, it will be assumed that the term recites "gene of claim X further comprising a DNA sequence centered at about position -10 in the promoter sequence, wherein said DNA sequence is TATAAT . . . ". Correction is required.

***Claim Rejections - 35 USC § 112, First Paragraph***

14. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

15. Claims 20-37 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This rejection, which was discussed at length in Paper No. 16, mailed on 2/12/2003, was previously applied to now cancelled claims 12 and 14. It is now applied to newly added claims 20-37 for the reasons of record and those set forth below.

16. Applicants argue that the Examiner concedes that the specification adequately discloses the production of coryneform bacteria having mutant promoters for the coryneform bacteria glutamate dehydrogenase, citrate synthase, isocitrate synthase, pyruvate dehydrogenase, and aconitase genes. Therefore, Applicants assert that the new claims recite subject matter that the Examiner has deemed

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adequately described and submit that the instant claims satisfy the written description requirements of 35 USC 112 first paragraph (Reply filed on 8/12/2003).

17. Applicant's arguments have been fully considered but are not deemed persuasive to avoid the rejection of new claims 20-37. While the new claims are now limited to (1) genera of genes encoding glutamate dehydrogenases, citrate synthases, isocitrate synthases, pyruvate dehydrogenases, or aconitases, wherein said genes are linked to a genus of promoters comprising specific DNA sequences at specific locations (see Claim Rejections under 35 USC 112, second paragraph for claim interpretation), and (2) genera of coryneform bacteria comprising the genes of (1), the specification fails to provide the structures of all the genes encoding glutamate dehydrogenases, citrate synthases, isocitrate synthases, pyruvate dehydrogenases, and aconitases encompassed by the claims, as well as the structures of all the promoters encompassed by the claims. It is noted that the claims are not limited to genes from coryneform bacteria but rather to genes from any organism. The genera of genes and promoters claimed is extremely large and can encompass genes/promoters of diverse structure. While a sufficient written description of a genus of DNAs may be achieved by a recitation of a representative number of DNAs defined by nucleotide sequence or a recitation of structural features common to members of the genus, which features constitute a substantial portion of the genus, in the instant case, there are no structural limitations recited for the genes encompassed by the claims and the structural limitations recited regarding the promoters (i.e. hexamers) do not constitute a substantial portion of the genus as the remainder of any nucleic acid comprising said structural elements is completely undefined and the specification does not define the remaining structural features for members of the genus to be selected. Many structurally unrelated polynucleotides are encompassed by these claims. The specification only a few species which is insufficient to put one of ordinary skill in the art in possession of all attributes and features of all species within the claimed genera. Thus, one cannot reasonably conclude that the claimed invention is adequately described.



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18. Claims 20-37 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a coryneform bacterium glutamate dehydrogenase gene linked to a mutated coryneform bacterium promoter comprising the DNA sequences recited in the claims, does not reasonably provide enablement for (1) any gene encoding glutamate dehydrogenase, citrate synthase, isocitrate dehydrogenase, pyruvate dehydrogenase, or aconitase linked to any promoter comprising the DNA sequences recited in the claims, and (2) a coryneform bacterium comprising the genes of (1). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. This rejection, which was discussed at length in Paper No. 16, mailed on 2/12/2003, was previously applied to now cancelled claims 12 and 14. It is now applied to newly added claims 20-37 for the reasons of record and those set forth below.

19. Applicants argue that the Examiner recognizes the enablement of a coryneform bacterium glutamate dehydrogenase gene linked to a mutated coryneform bacterium promoter comprising the hexamers recited in previous claim 4. Therefore, according to Applicants, new claims 20-37 recite subject matter which is fully enabled (Reply filed on 8/12/2003).

20. Applicant's arguments have been fully considered but are not deemed persuasive to avoid the rejection of new claims 20-37. As indicated above, the scope of the claims encompass genes encoding any glutamate dehydrogenase, citrate synthase, isocitrate synthase, pyruvate dehydrogenase, or aconitases, wherein said genes are linked to any promoter which comprises specific DNA sequences, wherein said DNA sequences are centered at specific locations within the promoter. See Claim Rejections under 35 USC 112, second paragraph for claim interpretation. The specification provides no disclosure of the structures of all the genes/promoters encompassed by the claims nor does it provide the critical structural elements required in any gene to encode the enzymes recited in the claims. As indicated in Paper No. 16, the state of the art, as evidenced by Bork, Broun et al., Seffernick et al., Van de Loo et

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al., teaches the unpredictability of isolating genes encoding enzymes of similar function by sequence homology. It is also reiterated herein that there is no evidence provided which would suggest that expression of any of the genes recited (from any source) wherein said genes are linked to any promoter comprising the DNA sequences recited would result in increased production of glutamic acid. Therefore, in view of the lack of relevant examples, the amount of information provided, the lack of knowledge about the critical structural elements required to encode the desired enzymes, and the unpredictability of the art in regard to function based on structural homology, one cannot reasonably conclude that the full scope of the claims is enabled by the specification.

### ***Claim Rejections - 35 USC § 102***

21. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.
22. Claim 12 was rejected under 35 U.S.C. 102(b) as being anticipated by Baggio et al. This rejection has been discussed at length in Paper No. 16, mailed on 2/12/2003.
23. Claim 12 was rejected under 35 U.S.C. 102(b) as being anticipated by Teller et al. This rejection has been discussed at length in Paper No. 16, mailed on 2/12/2003.
24. In view of Applicant's cancellation of claim 12, this rejection is hereby withdrawn. New claims 20-36 are directed to a gene encoding a glutamate dehydrogenase, citrate synthase, isocitrate synthase, pyruvate dehydrogenase, or aconitase, wherein said genes are linked to promoters which comprise specific DNA sequences centered at about positions -35 and/or -10 within the promoter. Neither Baggio et al. nor Teller et al., alone or in combination, teach a gene encoding a glutamate dehydrogenase, citrate synthase, isocitrate synthase, pyruvate dehydrogenase, or aconitase wherein said gene comprises a promoter, and wherein said promoter contains the recited hexamers in the specific locations recited in the claims. Therefore, these references are not deemed prior art against claims 20-36.

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**Conclusion**

25. No claim is in condition for allowance.

26. Applicant's amendment canceling claims 1-19 and adding claims 20-37 necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.


27. Certain papers related to this application may be submitted to Art Unit 1652 by facsimile transmission. The FAX number is (703) 872-9306. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6(d)). NOTE: If Applicant submits a paper by FAX, the original copy should be retained by Applicant or Applicant's representative. **NO DUPLICATE COPIES SHOULD BE SUBMITTED**, so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Delia M. Ramirez whose telephone number is (571) 272-0938. The examiner can normally be reached on Monday-Friday from 8:30 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Ponnathapura Achutamurthy can be reached on (571) 272-0928. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1234.

Delia M. Ramirez, Ph.D.  
Patent Examiner  
Art Unit 1652

DR  
February 3, 2004

  
**REBECCA E. PROUTY**  
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